Remarks

Claims 1, 3-6, 8 to 21 and 25 to 28 are currently pending in this application after claims 13 and 24 have been canceled and claims 25 to 28 have been added. Only claims 1, 11, and 25 are in independent form. Amendments to the claims were introduced to further clarify the claim language.

Interview

Applicant and his representative would like to thank Examiner Afremova for granting a further interview on May 10, 2005 to seek resolution of this application.

Memorandum of Interview

On May 10, 2005 Examiner Afremova, Prof. Sitar and the undersigned held a personal interview. The Bianchi reference as well as Boyer were discussed during the interview. Prof. Sitar explained the differences between the currently claimed invention and this prior art. It was in particular pointed out that the prior art does not teach a decrease in density in of NRBCs and increase in density of monocytes and lymphocytes which allows for a substantial separation of these cell types. This separation is in turn allows one to ascertain the presence of fetal NRBCs in a low cell density fraction comprising NRBCs. It was also pointed out that the cell separation method disclosed by the prior art involved several separation steps each of which was associated with a loss in fetal cells, which are present in maternal blood only in very low numbers. During the interview the 35 USC §112 rejections that were made in the context of claim 1 were discussed as well as the need to formally submit the declarations by Prof. Sitar previously submitted in draft to overcome the rejection of claim 1. Alternative wording for the claim 11 was also discussed.

New claims 25, 26 and 27

New claim 25 is supported, for example, by the Example on page 7, line 7 to 9,

Table 2 and page 10, line 15 to 23. Se also page 5, lines 10 to 15.

New claims 26 and 27 are supported, for example, by Table 3 which shows that no more than 13000 nucleated cells had to be analyzed for reliable genetic investigation. Applicant directs the Office's attention to the column entitled "Nucleated cells analyzed by FISH" in combination with the last two columns in Table 3. The last two columns show that in each of the batches of "nucleated cells analyzed by FISH," e.g., 13767 for sample "PIN," there was a sufficient number of fetal cells for reliable genetic investigation.

Claim 25 is phrased in functional terms. Applicant submits that functional limitations have been found acceptable (MPEP §2173.05(g)). Applicant also notes that the functional language renders the claim relatively broad. However, breadth does not render a claim indefinite (MPEP §2173.04). In fact, generally an invention can be claimed as broadly as the prior art allows as long as the other requirements for patentability are met. Applicant also notes that different parts of the specification including the abstract, define non-physiological media by what they do rather than by what they are (in this context, please see also claim 1 as originally filed). Applicant submits that the specification does not indicate that without specifically prescribed physiological conditions the invented process would not work (please compare *In re Mayhew*, 527 F.2d 1229, 1233, 188 USPQ 356, 358 (C.C.P.A. 1976)).

In paragraph 1 on page 2, the Office rejected claims 1, 11 and 24 under 35 U.S.C. §112, second paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In particular, the claims were rejected for being unclear as to what the final product is.

The independent claims were amended to clarify what the final product is. For example, in the case of claim 1, a low cell density fraction comprising fetal NRBCs.

Support for this amendment can be found, for example, on page 10, lines 16 to 19 and elsewhere in the specification.

To further clarify claim 11, the limitations of claim 13 were incorporated into the claim. The claim now makes clear that NRBCs are separated in this method from monocytes and lymphocytes. The claims was further clarified in that it now refers to "causing **substantial** separation." Support for this amendment can be found, for example, on page 10, lines 16 to 19 and elsewhere in the specification.

In paragraph 2 on page 3, the Office rejected claims 10, 16, 20 and 21 under 35 U.S.C. §112, second paragraph as being unclear with regard to the meaning "a single separation device" and/or a "single centrifugation step" in view of the fact that the issue of cells that are separated/isolated was considered to be unclear.

Applicant refers to the amendments of the independent claims discussed above and submits that these amendments in combination with the amendments to claims 10, 16, 20 and 21 should fully address this rejection.

In paragraph 1 on page 3, the Office rejected claims 11 to 17, 21 and 24 under 35 USC §102(b) as being anticipated by Boyer.

Boyer discloses the enrichment of erythrocytes of fetal origin from maternal blood via selective hemolysis of maternal erythrocytes. After a hemolytic reaction at a low pH, the preparation is centrifuged. Intact erythrocytes are removed by sedimentation. After removing the supernatant, the cells are resuspended in BSA in 0.15M NaCl, followed by transfer into and centrifugation in another tube and optionally (if the number of intact erythrocytes is < 20,000) followed by yet another transfer and centrifugation step.

Claim 11 requires:

> providing peripheral maternal blood comprising nucleated red blood cells (NRBCs) and monocytes and lymphocytes having overlapping density distribution profiles;
>
> . . .
>
> causing substantial separation of said NRBCs from said monocytes and lymphocytes by subjecting said non-physiological tissue culture mixture to centrifugation in a discontinuous density gradient,
>
> wherein said NRBCs are present in a low density cell fraction.

(emphasis added)

Applicant respectfully submits that Boyer teaches an enrichment /separation of erythrocytes, which by definition have no nucleus. In contrast, the present invention is directed at the separation of nucleated red blood cells (NRBCs) from monocytes and lymphcytes. Thus, Boyer does not teach all elements of the claim as required for a rejection under 35 USC §102(b). Boyer uses the sediment in each of the centrifugation steps disclosed (compare also claim 16) for further transfer/ analysis. Boyer eventually analyzes the cells in the sediment. A teaching of a separation of NRBCs from monocytes and lymphocytes as required by the rejected claims is not taught, nor is a collection of a low density cell fraction containing NRBCs as required by claim 11. Thus, applicant submits that Boyer also does not teach these elements of the claim as required for a rejection under 35 USC §102(b).

In paragraph 2 on pages 4 and 5, the Office rejected all pending claims under 35 USC §102(a) as being anticipated by Cytometry, Vol. 35, No. 4, page 337-347 (April 1, 1999).

Applicant appreciates the Office willingness to withdraw this rejection by submission of the proposed declaration which was discussed during the telephone interview of 9/15/2004. Applicant also notes that the foreign priority claim to MI99A000652 has been perfected.

On pages 5 to 8, the Office continues to reject claims 1, 3-5, 7 and 8 under 35 U.S.C. §103(a) as being unpatentable over U.S. Patent No. 5,641,628 to Bianchi (hereinafter "Bianchi") in view of U.S. Patent No. 5,676,849 to Sammons et al. (hereinafter "Sammons"), U.S. Patent No. 5,432,054 to Saunders et al. (hereinafter "Saunders") and Guyton's Textbook of Medical Physiology.

Applicant respectfully directs the Office's attention to the revised declaration under 37 U.S.C. §1.132 which corresponds to the draft declaration previously submitted to the Office and which explains the distinctions between the present invention and Bianchi.

As discussed the response filed on June 30, 2004, the declaration clarifies that the addition of regular amounts of the anticoagulant ACD to blood as disclosed in

Bianchi, would not lower the pH to the range of 6.4 to 6.6 as claimed in the rejected claims. The declaration also outlines why Sammons does not disclose the claimed pH range by inherency.

Accordingly, applicant submits that Bianchi combined with the secondary references cited does not teach or suggest all the claim limitations as required for a rejection under 35 USC §103(a) (MPEP §2142). Applicant further submits that there is no suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify Bianchi or combine it with the teachings of the secondary references to arrive at the claimed invention. Finally, applicant submits that there is no reasonable expectation of success.

Applicant has amended the claims to overcome the Office's rejection under 35 USC §112, second paragraph.

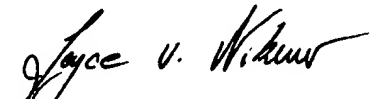
Applicant has also submitted the two declarations previously submitted in draft. Applicants believe that is view of this claim 1 should now be in condition for allowance. Claims 3 to 6 and 8 to 10 and 20, which are dependent on claim 1 should therefore also be in condition for allowance.

Applicant has shown above that claim 11 is not anticipated by Boyer. Accordingly, this claim should not be in condition for allowance. Claims 12, 14 to 19, 21 and 26, which are dependent on claim 11 should equally be in condition for allowance.

Reconsideration of the application is respectfully requested.

The Examiner is invited to call applicant's representative at the number listed below to further the completion of the prosecution this case.

Respectfully submitted,



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